

## **REMARKS**

The Office Action set forth the following rejections:

Claims 1-5 were rejected under 35 U.S.C. § 101 and § 112, first paragraph, as lacking utility; and

claims 4 and 5 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled.

No claim amendments are currently made.

### **§ 101 and § 112 utility rejections of claims 1-5**

The Section § 101 utility requirement has a low threshold. All that Applicants need to demonstrate is that the claimed invention has a well-established utility for some purpose, either explicitly or implicitly. The utility must be specific, substantial and credible. According to the MPEP, the "specific and substantial" requirement excludes "throw-away", "insubstantial" or "nonspecific" utilities. See, MPEP § 2107(II)(B)(1)(i). Moreover, an applicant needs to provide only one credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement. See, MPEP §2107(II)(B)(1)(ii).

#### **Credibility**

According to the MPEP, in most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101. Moreover, the asserted utility must be regarded as credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion. See, MPEP §2107.02(III)(B).

Applicants respectfully suggest that the asserted utilities of this invention (for example, the use of the claimed polypeptide as bait for identifying calpain

inhibitors selective for CAPN11, and subsequent use of the inhibitors in treatment of disorders associated with CAPN11 activity) are credible.

Applicants note that the Office Action appears to accept that Applicants' assertion that the polypeptide of SEQ ID NO: 2 is a calpain-family protease is credible. See, Office Action, page 6, line 5 in paragraph (B). However, the Office Action asserts that "the logic underlying Applicants' assertion of patentable utility is flawed." Applicants respectfully disagree. Because the Office Action's mistaken assertion rests on the premise that the claimed protein lacks a specific and substantial utility, Applicants will address this issue in the "Specific and Substantial Utility" section of the Remarks.

#### Specific and Substantial Utility

Applicants respectfully maintain that the utilities of the claimed invention are specific and substantial. The polypeptides claimed in the invention may be useful, for example, as a bait for identifying substances, which are able to inhibit enzymatic activity of the polypeptide. See, specification, page 4, lines 1-21.

A "specific" utility is specific to the subject matter claimed. The MPEP makes clear that the PTO should distinguish between situations where a specific use is disclosed and situations where it is not identified why the invention is considered useful. See, MPEP §2107.01(I)(A). While a general statement of diagnostic utility without disclosure of what condition can be diagnosed is insufficient to demonstrate specific utility, the specific utility is present where an applicant discloses a specific biological activity and reasonably correlates the activity to a disease condition.

A "substantial" utility defines a "real world" use. The MPEP states that "any reasonable use that an applicant has identified for the invention that can be

viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility." See, MPEP §2107.01(I)(B).

Applicants respectfully submit that the invention has specific and substantial utility. Applicants demonstrated that CAPN11 is most strongly expressed in testis. Also, Applicants determined the chromosome on which the human CAPN11 gene is located. Because it is known that calpains in other tissues are involved in certain processes, such as germ cell apoptosis and regulation of tissue-specific transcription factors, it is reasonable to suggest that CAPN11 may be involved in similar processes in testis. Moreover, the specification discloses that the claimed polypeptide may be used as a bait for identifying substances, which are able to inhibit enzymatic activity of the polypeptide. In turn, these inhibitors may be used for treatment of disorders associated with or linked to a non-physiologically elevated CAPN11 activity such as infertility in men. See, specification, page 4, lines 1-26.

These utilities are specific and substantial. It is not as if Applicants are claiming that polynucleotides or polypeptides might be useful in treating unspecified disorders, or that the protein has unspecified useful properties. In contrast, the application discloses a relation to specific processes, such as germ cell apoptosis. A person skilled in the art knows that cysteine proteases are involved in apoptosis. See, for example, *Billing, H., Chun, S.-Y., Eisenhauer, K. and Hsueh A. J. W., Human Reprod. Update, Vol. 2, No. 2, pp. 103-107 (1996)*. It has been shown that proteases play a great role in apoptosis. See, for example, *Martin, S. J. and Green, D. R., Cell, Vol. 82, pp. 349-352 (1995)*. The use of the invention to advance treatment of the specified disease (for example, male infertility) is providing a public benefit. Moreover, Applicants respectfully maintain that the use of inhibitors of CAPN11 activity to treat infertility inherently demonstrates utility for the protein CAPN11 itself.

Accordingly, the present application identifies a specific and substantial utility for the invention and discloses enough information about the invention to make its usefulness immediately apparent to those familiar with the technological field of the invention.

Response to the Office Action's Arguments

Applicants will refer to the (A) to (I) nomenclature of the Office Action. Applicants re-incorporate by reference all of the arguments made in previous Responses. The additional comments are provided below.

(A) Applicants respectfully disagree with the Office Action's position that the polypeptide of SEQ ID NO:2 does not have a specific, substantial, and credible utility for the reasons above and also provided in (B) through (I) of this section.

(B) While it is true that the calpain family is large, it does not negate the asserted utilities of the claimed polypeptide as, for example, bait for identifying calpain inhibitors selective for CAPN11, and subsequent use of the inhibitors in treatment of disorders associated with CAPN11 activity. While the Office Action asserts that the specification fails to provide evidence of a specific and substantial utility for the protein of SEQ ID NO: 2, Applicants respectfully maintain that the specification provides such evidence in disclosing the polypeptide, identifying it as belonging to the calpain family of proteins, and suggesting its specific uses. It is within a skill of the art to use the claimed polypeptide for the asserted utilities; and thus, the asserted utility is credible.

(C) Applicants respectfully insist that the identification of chromosome localization of CAPN11 provides a specific and substantial utility. As Applicants have demonstrated, calpains are involved in certain processes, such as apoptosis and regulation of tissue-specific transcription factors. Thus, a skilled

artisan would conclude that, more likely than not, the claimed polypeptide is involved in similar processes.

Applicants respectfully disagree with the Office Action's assertion that the genus of cysteine proteases is too large to conclude that the claimed polypeptide is likely involved, for example, in apoptosis or may have utility in the treatment of male fertility. It is reasonable to deduce that on the basis of its preferential expression in testis, the claimed CAPN11 is likely "involved in regulating key signal transduction events and processes of cytoskeletal remodeling during meiosis, spermiogenesis and sperm function." See, Ben-Aharon, at 772, right column.

(D) Applicants respectfully maintain that it is well within a skill in the art to arrive at substrates and design proper assay conditions. Applicants' position is that the application's disclosure is sufficient to enable a skilled artisan to identify an inhibitor of CAPN11 activity. Applicants respectfully point out that claims do not recite treatment of diseases; accordingly, Applicants are not required to demonstrate that treatment of diseases is enabled under §112 standard.

(E) It is respectfully submitted that for all of the above reasons, preferential expression of CAPN11 in testis, together with other evidence of utility submitted by Applicants, provides a specific and substantial utility for the claimed polypeptide. Applicants again refer to Ben-Aharon et al which states that CAPN-11 is likely involved in regulating key signal transduction events and processes of cytoskeletal remodeling during meiosis, spermiogenesis, and sperm function." See, Ben-Aharon, at 772, right column. The Office Action does not cite any prior art contradicting the conclusions of this reference. Thus, it is more likely than not that a skilled artisan would conclude with Ben-Aharon's conclusions.

(F) The Office Action presents the same arguments as in (D). Applicants respectfully refer to the arguments in (D).

(G)-(I) Applicants respectfully maintain that no further evidence needs to be submitted to demonstrate a patentable utility. Honbou et al supports the Applicants' position that CAPN11 is reasonably related to treatment of fertility. Contrary to the Office Action's assertion, Applicants did not "leave the work of obtaining evidence to the public." Based on the body of scientific knowledge about calpain family of enzymes, the public would have understood from the Applicants' disclosure the utility of CAPN11. Honbou et al further proves that the asserted utility is more likely to be true.

#### **§ 112, written description rejections of claims 4 and 5**

The Office Action rejected claims 4 and 5 as containing subject matter which was not described in the specification in a way as to reasonably convey to a skilled worker that the inventors at the time of the application was filed had possession of the claimed invention.

Applicants respectfully disagree. The Examiner's attention is again directed to page 4 of the application where a CAPN11 selective compound is defined as a compound that selectively blocks the activity of CAPN11 at least 10-fold, preferably 25-fold more than it blocks the activity of other calpains. This would clearly lead one of skill in the art to conclude that a method for identifying an inhibitor of the particular protein is taught. As already mentioned above, it is well known for a person skilled in the art that the enzyme activity can be determined by time dependent measurement of substrate and product concentrations. On page 4, the specification clearly teaches that the enzyme activity of CAPN11 is a Ca-dependent protease activity. This would clearly lead


one of skill in the art to conclude that a method for identifying an inhibitor of this particular protein is taught.

Thus, a skilled worker would have clearly concluded that Applicants had possession of the invention as defined in claims 4 and 5. Accordingly, this rejection should be withdrawn.

Favorable consideration of claims 1-5 is respectfully requested.

Respectfully submitted,

Date: June 27, 2008



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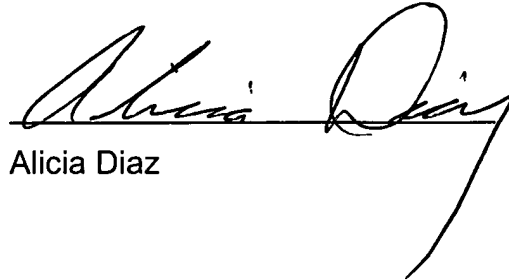
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CERTIFICATE OF MAILING

I hereby certify that this Paper and associated documents is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on **June 27, 2008**.



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